# EXHIBIT III

*IN THE UNITED STATES PATENT AND TRADEMARK OFFICE*

Applicant: William R. Wilson et al.

Title: Anti-Cancer Combinations

Appl. No.: 10/790,943

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Examiner: James D. Anderson

Art Unit: 1614

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**CERTIFICATE OF ELECTRONIC TRANSMISSION**
I hereby certify that this paper is being electronically transmitted to the United States Patent and Trademark Office, Alexandria, Virginia via EFS-Web on the date below.

Julie Costello
(Printed Name)

(Signature)

July 30, 2009
(Date of Transmission)

**DECLARATION OF HAKIM DJEHA**

Mail Stop AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Hakim Djeha, hereby declare that:

1. I earned a PhD in Immunology from the University of Glasgow, UK, in 1990. Attached is my curriculum vitae (Exhibit A).

2. I have been an employee of Antisoma, since October 2004. During this period, I have worked extensively in the field of combination of DMXAA and gemcitabine for the treatment of cancer. I am familiar with the present application and the claimed invention.

3. I have reviewed the present application, the Office Action and the art cited therein related to the rejection of claims 1-4, 7-8, 11-13, 16-17 and 20-21 under 35 U.S.C. §103(a) as

being unpatentable over Peters *et al.* (Pharmacology & Therapeutics, 2000, vol. 87, pages 227-253), Grindley *et al.* (US Patent No. 5,464,826) and van Moorsel *et al.* (Biochemical Pharmacology, 1999, vol. 57, pages 407-415) in view of Siemann *et al.* (Proceedings of the American Association for Cancer Research, 2000, vol. 41, page 525) and Pruijn *et al.* (Cancer Chemother. Pharmacol., 1997, col. 39, pages 541-546); and claims 1-4, 7-8, 11-13, 16-17 and 20-21 under 35 U.S.C. § 103(a) as being unpatentable over Davis et al. (WO 00/48591) in view of Peters et al. (Pharmacology & Therapeutics, 2000, vol. 87, pages 227-253).

4. My prior Declaration established a synergistic response to the administration of DMXAA in combination with gemcitabine as compared to DMXAA alone. The data was evaluated by the Fractional Product method as outlined in the prior Declaration. Using the statistical method as described below, the response to administration of DMXAA in combination with gemcitabine in a clinically relevant animal model is established to be statistically significant (P=0.038).

5. The data presented in the prior Declaration showed that significant anti-tumor response in various human xenograft models grown in the nude mouse was obtained at doses of DMXAA approaching the maximum tolerated dose following a standard schedule of once every 4 days for 3 times (days 0, 4 and 8). A dose of 18 mg/Kg was used for treatment since a dose of 21 mg/Kg administered to the MF1 nude mice would be close to the maximum tolerated dose (MTD) and prior experiments showed that a dose of 21 mg/Kg was toxic to the mice. Thus, the dose of 18 mg/Kg was administered to reduce anticipated toxicity. Only two doses of 18 mg/Kg (days 0 and 4) were administered to the MF1 nude mice also to avoid toxicity

6. To evaluate whether the data submitted in my prior Declaration showed a statistically significant response, the data was analyzed using the Mann-Whitney Rank Sum Test:
Normality Test: Passed (P > 0.050)
Equal Variance Test: Passed (P = 0.151)

| Group | N | Missing | Median | 25% | 75% |
|---|---|---|---|---|---|
| DMXAA (day 4) | 10 | 0 | 1.921 | 1.230 | 2.484 |
| DMXAA + GEM (Day 4) | 10 | 0 | 1.341 | 0.458 | 1.43 |

T = 133.000 n(small)= 10 n(big)= 10 (P = 0.038)
Median is compared to day 0.

7. In view of the above analysis, it is my opinion that combination treatment with a single intravenous dose of DMXAA (18 mg/kg) and gemcitabine (240 mg/kg) to mice bearing NCI-H460 xenografts, as presented in the Declaration filed on March 23, 2009, resulted in a synergy in relative tumor growth inhibition during the duration of treatment when compared with either agent alone. The difference in the median values between the two groups is greater than would be expected by chance. Therefore, there is a statistically significant difference (P = 0.038) between the administration of DMXAA alone and DMXAA in combination with gemcitabine. However, as soon as the treatment was stopped (> day 8) the combination treatment was additive only. No treatment was given on day 8 because toxicity concerns.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Welwyn Garden City, (UK), this 23rd day of July, 2009.

Hakim Djeha